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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

TXR.No. 0050483

MEMORANDUM February 21, 2002

SUBJECT: **Iprovalicarb** Revised Quantitative Risk Assessment (Q_1^*) Based On
Hsd/WIN:WU(SPF) Rat Chronic Dietary Study With $^3/_4$'s Interspecies Scaling Factor

P.C. Code 098359

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Introduction

An initial Quantitative Risk Assessment (Q_1^*) based on a Hsd/WIN:WU(SPF) Rat Chronic Dietary Study of Iprovalicarb, dated November 8, 2001 (TXR. No. 0050267) was made by L. Brunsman. This memorandum includes results of that previous analysis and that of two additional types of tumors which occurred in female rats: uterine mixed muellerian tumors and urinary bladder transitional cell papilloma tumors.

The most potent unit risk, Q_1^*(mg/kg/day)$^{-1}$, for Iprovalicarb is 4.47 x 10^{-4} in human equivalents based on female rat thyroid gland follicular cell adenoma and/or carcinoma combined tumor rates. The dose levels used from the 106-week dietary study were 0, 31.7, 326.3, and 1379.7 mg/kg/day of Iprovalicarb. The corresponding tumor rates were 0/49, 0/49, 2/48, and 3/48, respectively.

Background

All unit risks have been converted from animals to humans by use of the $^3/_4$'s scaling factor (Tox_Risk program, Version 3.5, K. Crump, 1994)[1]. For the conversion to human equivalents, weights of 0.35 kg for the rat, 70 kg for humans and the use of 106 weeks for the rat life-span were used.

It is to be noted that the Q_1^* $(mg/kg/day)^{-1}$ is an estimate of the upper bound on risk and that, as stated in the EPA Risk Assessment Guidelines, "the true value of the risk is unknown, and may be as low as zero."

Dose-Response Analysis

The statistical evaluation of mortality indicated a significant decreasing trend with increasing doses of Iprovalicarb in male rats, but there were no statistically significant incremental changes in mortality with increasing doses of Iprovalicarb in female rats (Iprovalicarb Revised Qualitative Risk Assessment Based On Hsd/WIN:WU(SPF) Rat Dietary Study, V. Fornillo, 2/21/2002, TXR No. 0050482). Therefore, the estimate of unit risk, Q_1^*, for the males was obtained by the application of the time-to-tumor Weibull model and the estimate of unit risk, Q_1^*, for the females was obtained by the application of the Multi-Stage model (Tox_Risk program, Version 3.5, K. Crump, 1994).

Male rats had significant increasing trends in bone (femur) osteosarcomas, bone (lower jaw) osteosarcomas, and nasal cavity chondrosarcomas, all at $p < 0.05$. Male rats also had a significant increasing trend in bone (femur) osteosarcomas and/or bone (lower jaw) osteosarcomas combined at $p < 0.01$. There was a significant difference in the pair-wise comparison of the 20000 ppm dose group with the control for bone (femur) osteosarcomas and/or bone (lower jaw) osteosarcomas combined at $p < 0.05$.

Female rats had a significant increasing trend in thyroid gland follicular cell adenomas and/or carcinomas combined at $p < 0.05$. There were no significant differences in the pair-wise comparisons of the dosed groups with the controls.

Additional Q_1^* Calculations

The unit risk, Q_1^* $(mg/kg/day)^{-1}$, of Iprovalicarb based upon **male rat bone osteosarcoma (combined femur and lower jaw)** tumor rates is 2.43×10^{-4} in human equivalents. The dose levels used from the 106-week dietary study were 0, 26.0, 262.5, and 1109.6

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[1]See memo - Deriving Q_1^*s Using the Unified Interspecies Scaling Factor, P.A. Fenner-Crisp, Director, HED, 7/1/94.

mg/kg/day of Iprovalicarb. The corresponding tumor rates were 0/59, 0/60, 0/56, and 3/60, respectively.

The unit risk, Q_1^* $(mg/kg/day)^{-1}$, of Iprovalicarb based upon **male rat nasal cavity chondrosarcoma** tumor rates is 2.06×10^{-4} in human equivalents. The dose levels used from the 106-week dietary study were 0, 26.0, 262.5, and 1109.6 mg/kg/day of Iprovalicarb. The corresponding tumor rates were 0/35, 0/37, 0/41, and 1/41, respectively.

The unit risk, Q_1^* $(mg/kg/day)^{-1}$, of Iprovalicarb based upon **female rat uterine mixed muellerian** tumor rates is 3.13×10^{-4} in human equivalents. The dose levels used from the 106-week dietary study were 0, 31.7, 326.3, and 1379.7 mg/kg/day of Iprovalicarb. The corresponding tumor rates were 0/49, 0/49, 1/48, and 2/48, respectively.

The unit risk, Q_1^* $(mg/kg/day)^{-1}$, of Iprovalicarb based upon **female rat urinary bladder transitional cell papilloma** tumor rates is 2.09×10^{-4} in human equivalents. The dose levels used from the 106-week dietary study were 0, 31.7, 326.3, and 1379.7 mg/kg/day of Iprovalicarb. The corresponding tumor rates were 0/49, 0/48, 0/48, and 2/48, respectively.